Primary Prevention of Cardiovascular Disease

A LOT HAS CHANGED IN THE PAST 5 YEARS

Julie K. Gammack, MD CMD FACP

Saint Louis University School of Medicine

Learning Objectives

By the end of the presentation, participants will be able to:

- Define primary, secondary and tertiary prevention
- List primary prevention recommendations for cardiovascular disease
- Describe how recommendations may apply to the older population

Speaker Disclosures

I have no relevant financial relationships to disclose.

I am not a cardiologist.

Case 1

79 yo Caucasian female, moderate dementia, osteoporosis, residing in NH. Never smoker. Ambulates with wheelchair. DMII diet controlled without complications. On donepezil, alendronate, vitamin D. Weight 74 kg; BMI 26; BP 132/84; TC 180; HDL 50; LDL 110; Hgb A1c 7.2

➢ **10 yr ASCVD 43%**

- 1° vs 2° prevention?
- Lifestyle modifications?
- HTN Rx?
- T2DM Rx?
- ASA?
- Statin?

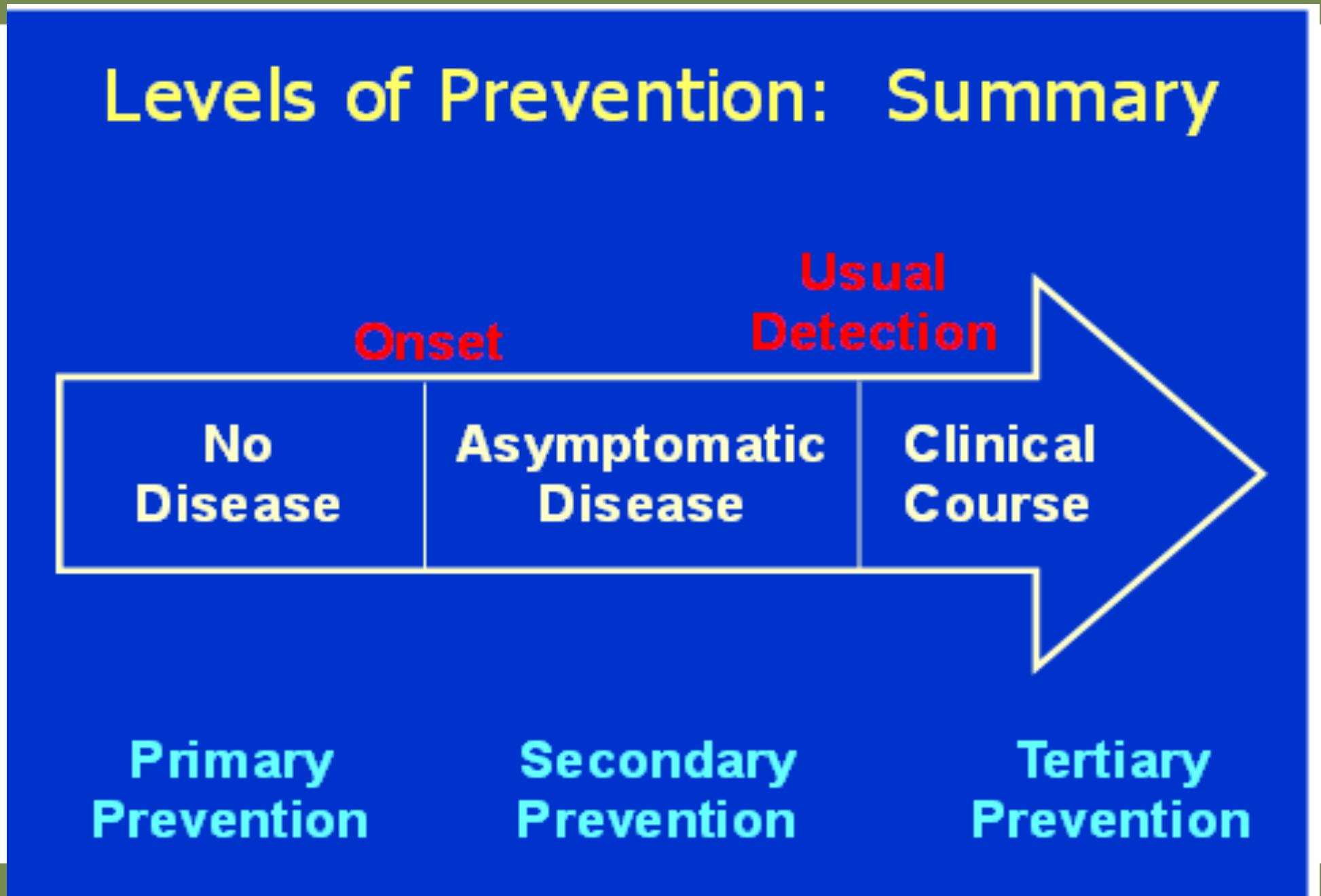
Case 2

72 yo Caucasian female, residing in the community. Never smoker. Bipolar, seizure disorder, ambulatory with recurrent falls. On antipsychotic, sertraline, levetiracetam. Weight 65 kg; BMI 22; BP 130/74; TC 210; HDL 60; LDL 126

➢ **10 yr ASCVD 12%**

- Lifestyle modifications?
- HTN Rx?
- ASA?
- Statin?

Disease Prevention



Guidelines & Clinical Documents

acc.org/Guidelines

2021

Coronary Artery Revascularization
JACC | PDF | Hub **NEW!**

Chest Pain
JACC | PDF | Hub **NEW!**

2020

Valvular Heart Disease
JACC | PDF | Hub

Hypertrophic Cardiomyopathy
JACC | PDF | Hub

2019

Innovations, Modifications, and Evolution of ACC/AHA Clinical Practice Guidelines

2016

Lower Extremity Peripheral Artery Disease
JACC | PDF | Hub

Dual Antiplatelet Therapy in Patients With Coronary Artery Disease (Focused Update)
JACC | PDF | Hub

2015

Surgery For Aortic Dilatation in Patients With Bicuspid Aortic Valves
JACC | PDF | Key Points to Remember

Clinical Practice Guideline Recommendation Classification System
JACC | PDF

Supraventricular Tachycardia

2013

Cardiovascular Risk
JACC | PDF | Hub

Lifestyle Management to Reduce Cardiovascular Risk
JACC | PDF | Hub

Overweight and Obesity in Adults
JACC | PDF | Hub

Heart Failure
JACC | PDF | Hub

Peripheral Arterial Disease (Lower Extremity, Renal, Mesenteric, and Abdominal Aortic)
JACC | PDF | Hub

2012

Primary Prevention

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, the **American Geriatric Society**, the American Society of Preventive Cardiology, and the Preventive Cardiovascular Nurses Association

- Full-text guidelines: ACC (www.acc.org); AHA (professional.heart.org)

Circulation. 2019;140:e596–e646. DOI: 10.1161/CIR.0000000000000678

Choosing Wisely®

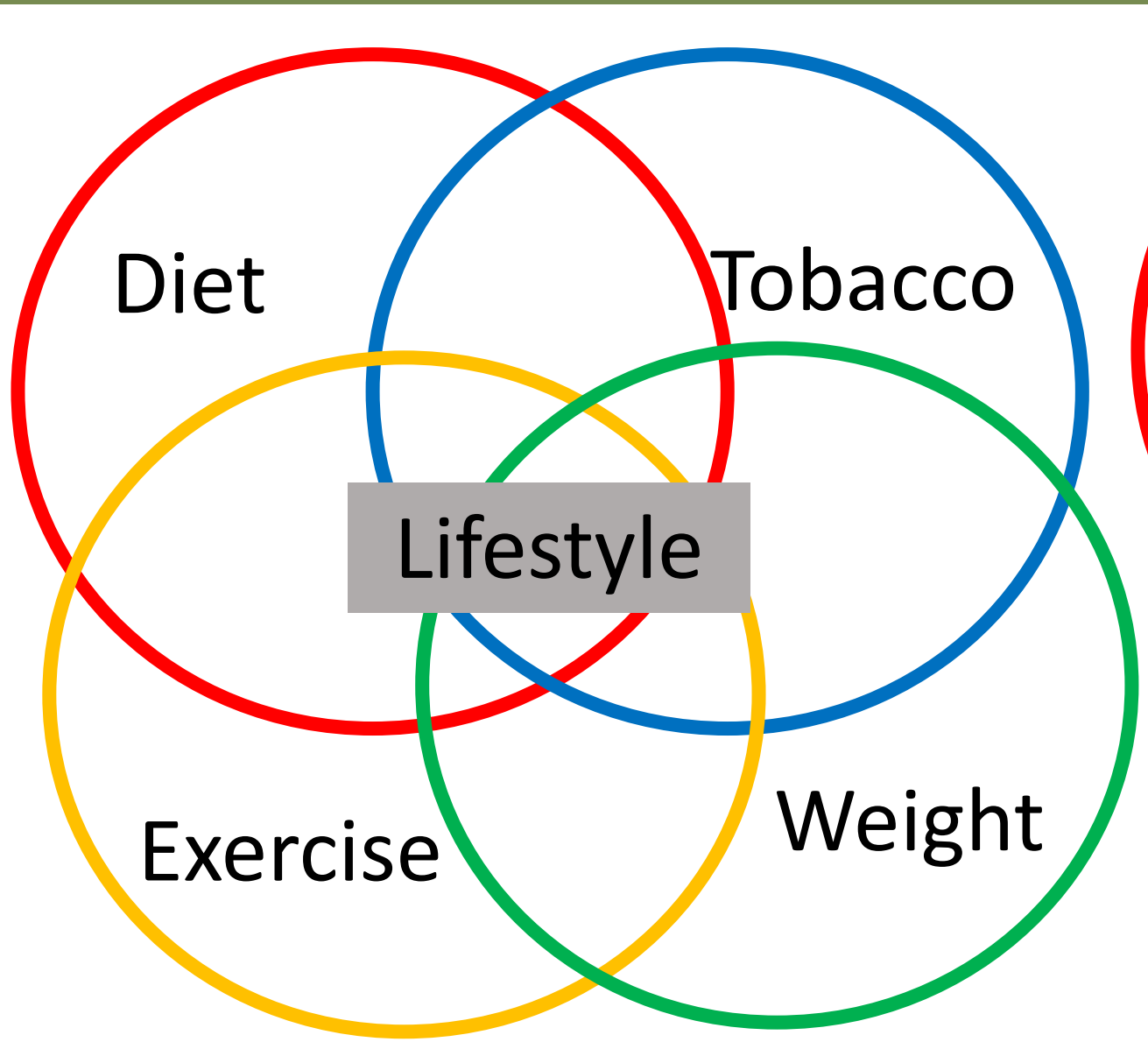
An initiative of the ABIM Foundation

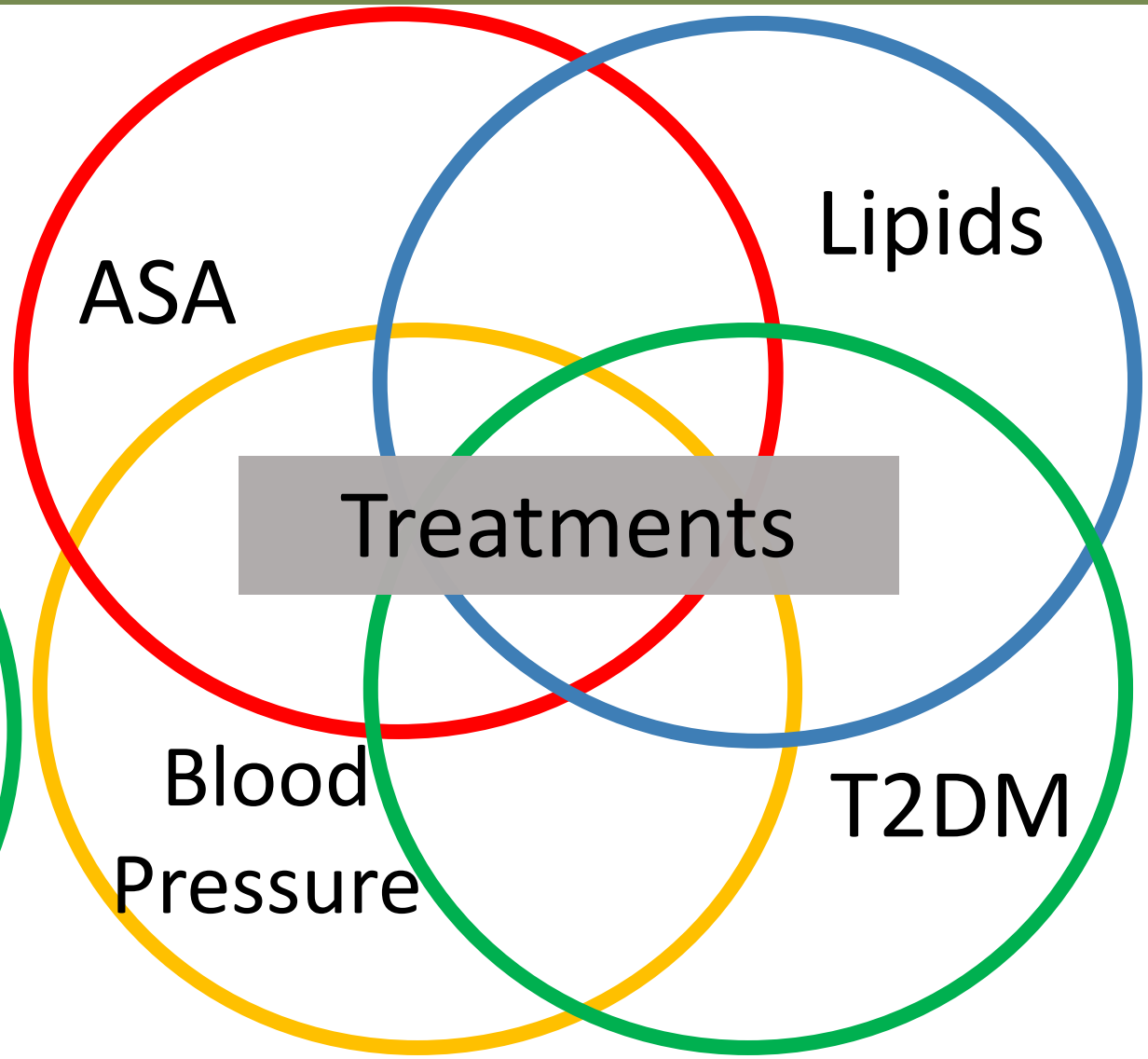
FRAIL
F (fatigue)
R (resistance-flight of stairs
A (aerobic-walk 1 block)
I (Illness >5)
L (loss of >5% weight in 6 mo)

Don't routinely prescribe **lipid-lowering medications** in individuals with a limited life expectancy.

Don't initiate aggressive **antihypertensive treatment** in frail individuals ≥60 years of age. For frail individuals with hypertension, multiple medical comorbidities, and limited life expectancy, use clinical judgment, patient/family preferences, and evaluation of risk/benefit in deciding on medication(s) and the intensity of control.

Primary Prevention





Lifestyle Therapies

Diet

- vegetables, fruits, whole grains, legumes
- healthy protein sources
- low-fat dairy, low-fat poultry,fish/seafood
- nuts, oils
- limited sweets, sugar-sweetened beverages, and red meats

Activity

- Avoid weight gain
- If overweight, promote weight loss
- aerobic activity 3-4x weekly x40 minutes
- Moderate+ intensity activity

Smoking cessation

Alcohol moderation

Obesity (Silver Spring). 2016 Oct;24(10):2232-9.

TABLE 8.1 Body Mass Index Classifications

BMI (kg/m^2)	Classification
<18.5	Underweight
18.5–24.9	Normal weight
25.0–29.9	Overweight
30.0–34.9	Obesity class 1
35.0–39.9	Obesity class 2
>40	Obesity class 3 (extreme obesity)

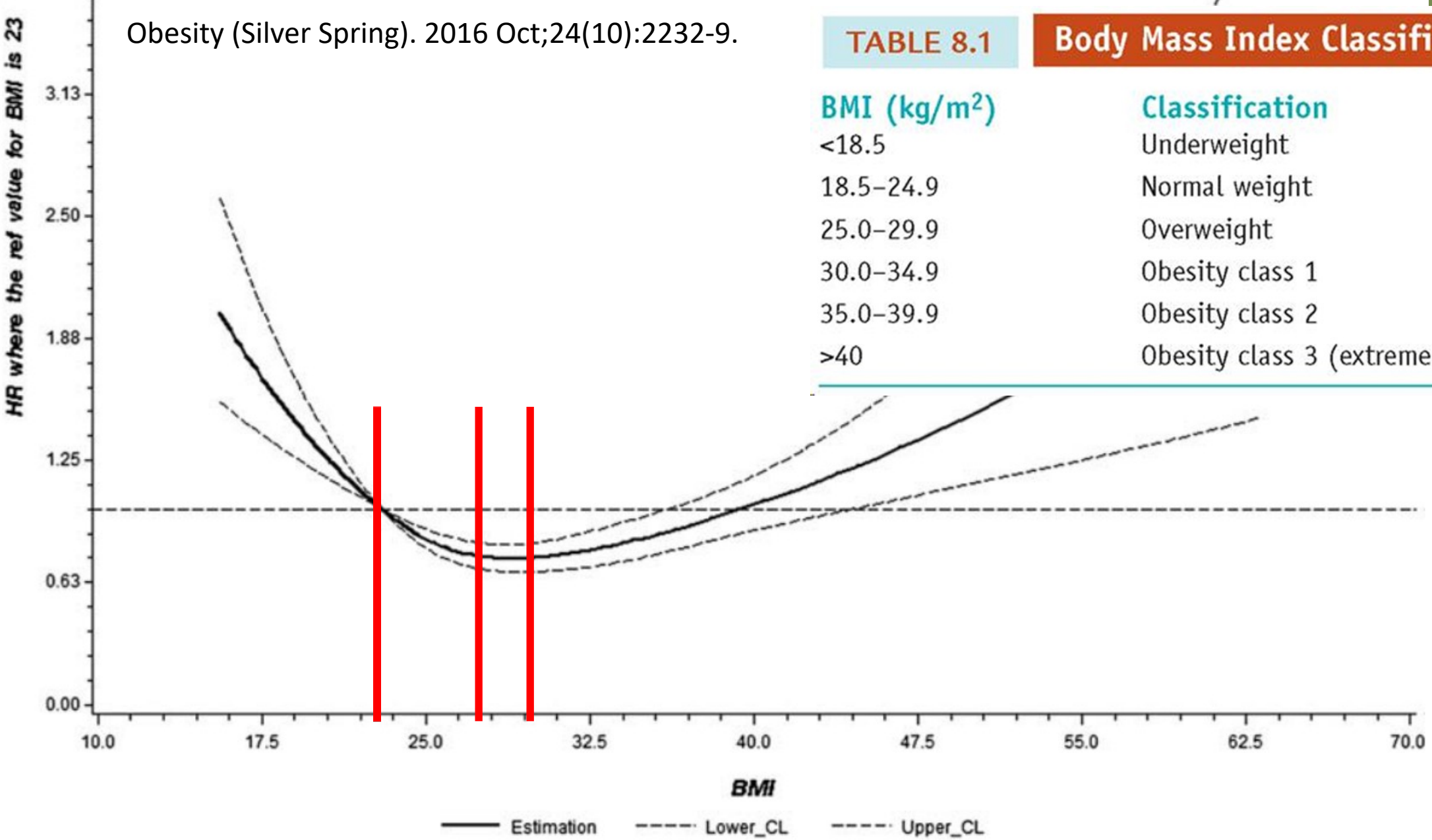


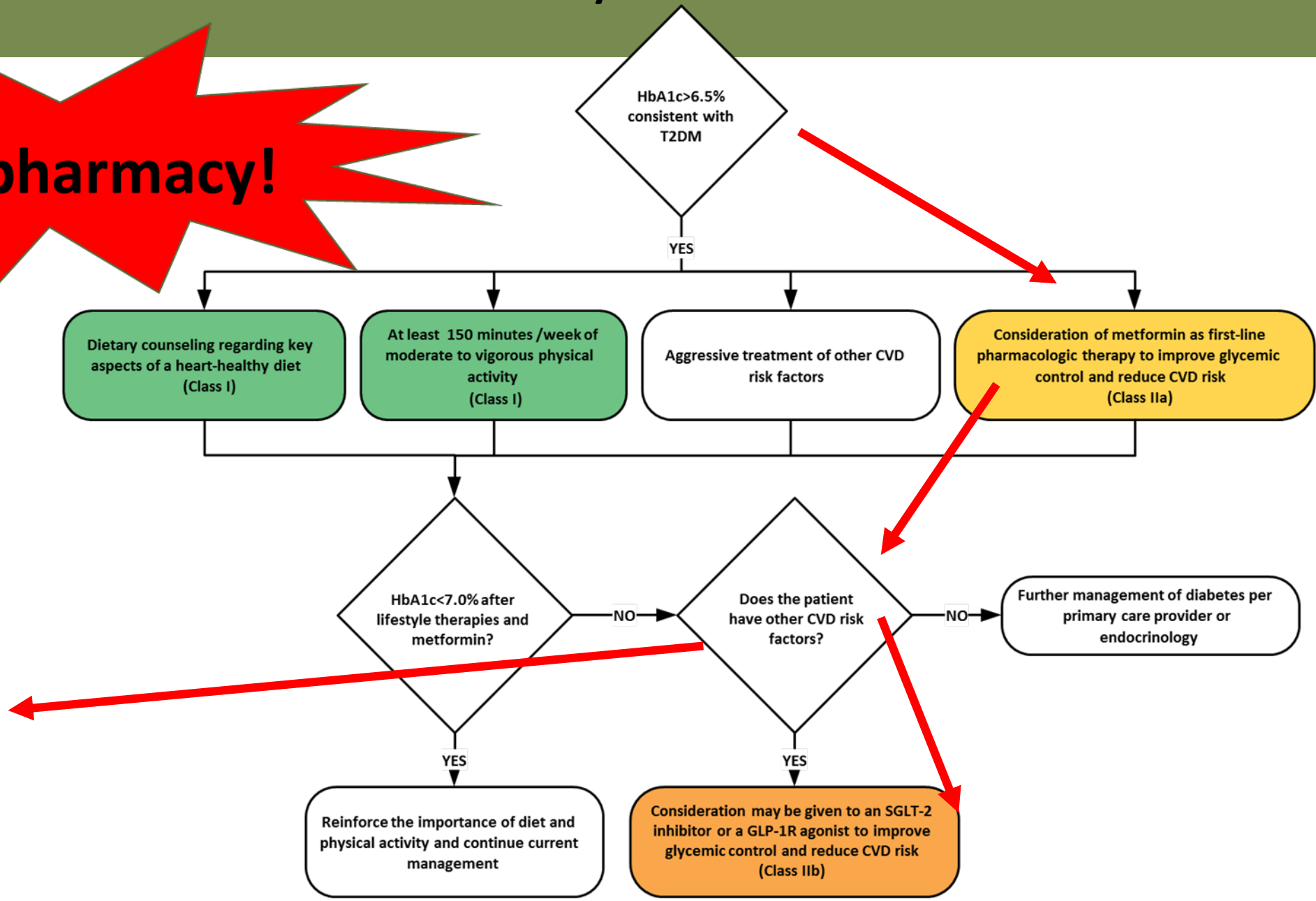
Figure 2 All-cause mortality in relation to body mass index (BMI): restricted cubic spline. HR/estimation

Fig. 2. Treatment of T2DM for Primary Prevention of CVD

Polypharmacy!

Risk enhancing factors

- FH premature ASCVD
- Primary HLD
- Metabolic syndrome
- CKD eGFR <60ml/min
- Chronic inflammation
- Ethnicity (south Asian)



Metabolic Syndrome: 3+ criteria

Table S2. Criteria for Clinical Diagnosis of the Metabolic Syndrome

Measure	Categorical Cut Points
Elevated waist circumference*	≥102 cm (40.1 in) (or 90 cm (35.4 in)) in males ≥88 cm (34.6 in) (or 80 cm (31.4 in)) in females
Elevated triglycerides (drug treatment for elevated triglycerides is an alternative indicator) †	≥175 mg/dL (2.0 mmol/L§)
Reduced HDL-C (drug treatment for reduced HDL-C is an alternative indicator) †	<40 mg/dL (1.0 mmol/L) in males <50 mg/dL (1.3 mmol/L) in females
Hypertension (antihypertensive drug treatment in a patient with a history of hypertension is an alternative indicator)	Systolic ≥130 and/or diastolic ≥85 mm Hg
Elevated fasting glucose (drug treatment of elevated glucose is an alternative indicator) ¶	≥100 mg/dL

Primary Prevention with T2DM

Recommendations for Adults With Type 2 Diabetes Mellitus		
COR	LOE	Recommendations
IIa	B-R	3. For adults with T2DM, it is reasonable to initiate metformin as first-line therapy along with lifestyle therapies at the time of diagnosis to improve glycemic control and reduce ASCVD risk.
IIb	B-R	4. For adults with T2DM and additional ASCVD risk factors who require glucose-lowering therapy despite initial lifestyle modifications and metformin, it may be reasonable to initiate a sodium-glucose cotransporter 2 (SGLT-2) inhibitor or a glucagon-like peptide-1 receptor (GLP-1R) agonist to improve glycemic control and reduce CVD risk.

SLGT-2: canagliflozin dapagliflozin and empagliflozin
GLP-1R: Dulaglutide, Exenatide Semaglutide Semaglutide .

AMERICAN COLLEGE of CARDIOLOGY

ASCVD Risk Estimator Plus

Estimate Risk

Referenced studies that support recommendations are summarized in Online Data Supplement 3.

COR	LOE	Recommendations
I	B-NR	1. For adults 40 to 75 years of age, clinicians should routinely assess traditional cardiovascular risk factors and calculate 10-year risk of ASCVD by using the pooled cohort equations (PCE).[S2.2-1,S2.2-2]

Current Age *

Age must be between 20-79

Sex *

Male | Female

Race *

White | African American | Other

Systolic Blood Pressure (mm Hg) *

Value must be between 90-200

Diastolic Blood Pressure (mm Hg) *

Value must be between 60-130

Total Cholesterol (mg/dL) *

Value must be between 130 - 320

HDL Cholesterol (mg/dL) *

Value must be between 20 - 100

LDL Cholesterol (mg/dL)

Value must be between 30-300

History of Diabetes? *

Yes | No

Smoker? *

Current | Former | Never

On Hypertension Treatment? *

Yes | No

On a Statin?

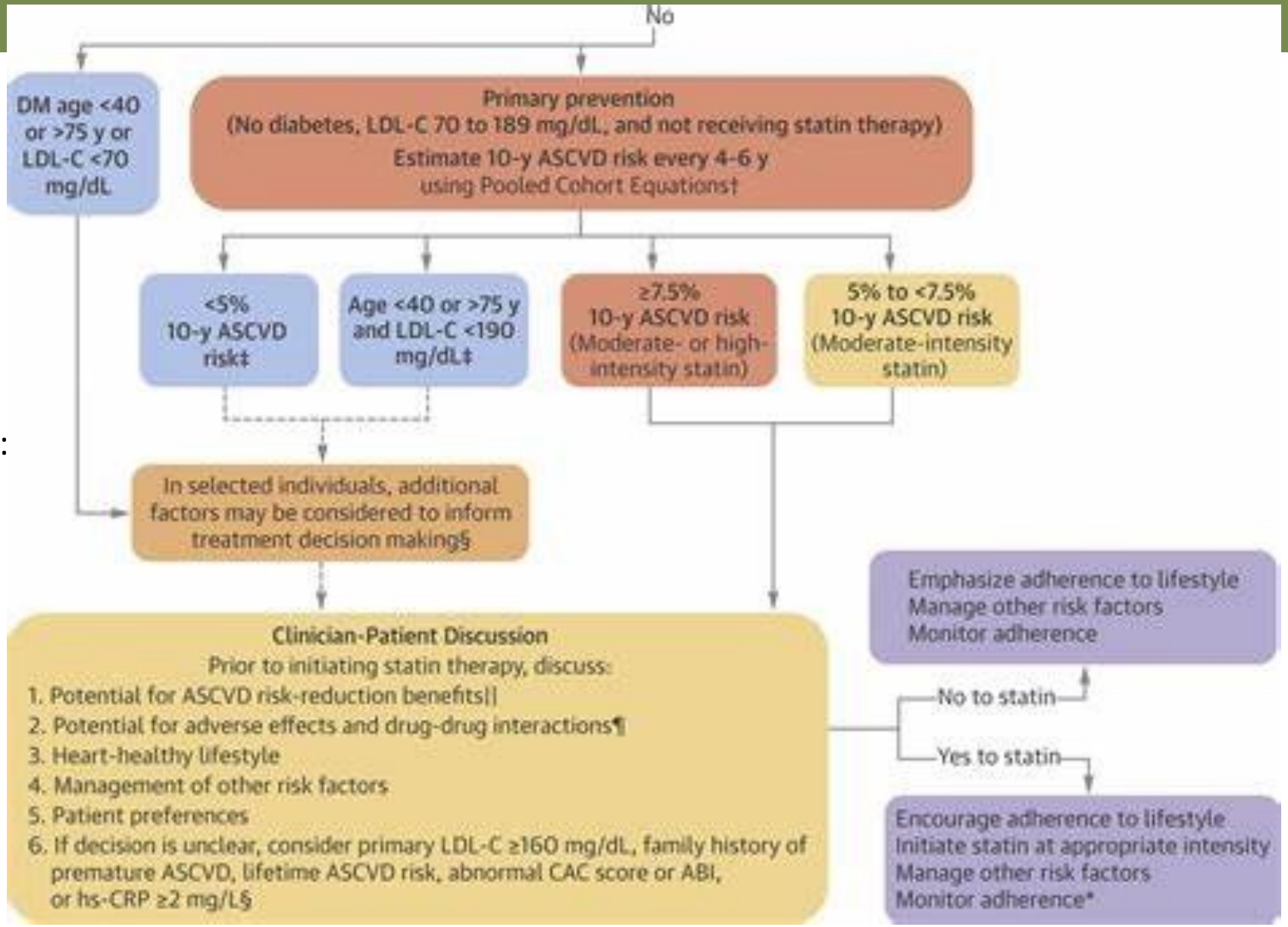
Yes | No

On Aspirin Therapy?

Yes | No

ASCVD Risk

**10-year risk for ASCVD is categorized as:
Low-risk (<5%)
Borderline risk (5% to 7.4%)
Intermediate risk (7.5% to 19.9%)
High risk (≥20%)



ASCVD Risk

Table 5. Diabetes-Specific Risk Enhancers That Are Independent of Other Risk Factors in Diabetes Mellitus

Risk Enhancers in Diabetic Patients
Long duration (≥10 years for T2DM[S4.3-61] or ≥20 years for type 1 diabetes mellitus[S4.3-16])
Albuminuria ≥30 mcg albumin/mg creatinine[S4.3-62]
eGFR <60 mL/min/1.73 m^2[S4.3-62]
Retinopathy[S4.3-63]
Neuropathy[S4.3-64]
ABI <0.9[S4.3-65,S4.3-66]

ASCVD Risk Enhancers:

- Family history of premature ASCVD
- Persistently elevated LDL-C ≥160 mg/dL (≥4.1 mmol/L)
- Chronic kidney disease
- Metabolic syndrome
- Conditions specific to women (e.g., preeclampsia, premature menopause)
- Inflammatory diseases (especially rheumatoid arthritis, psoriasis, HIV)
- Ethnicity (e.g., South Asian ancestry)

Lipid/Biomarkers:

- Persistently elevated triglycerides (≥175 mg/dL, (≥2.0 mmol/L))

In selected individuals if measured:

- hs-CRP ≥2.0 mg/L
- Lp(a) levels >50 mg/dL or >125 nmol/L
- apoB ≥130 mg/dL
- Ankle-brachial index (ABI) <0.9

Hypertension

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 71, NO. 19, 2018

American Geriatrics Society

CLINICAL PRACTICE GUIDELINE

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Hypertension Guidelines

2003

- Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC)
  - JNC-7: BP definitions

2013

- JNC-8: treatment recommendations

2013

- CPGs for CVD prevention transferred to the ACC/AHA

2014

- ACC, AHA +9 associations tasked to develop new HTN CPGs

2017

- New HTN CPG

Table 4. Recommendations for Nonpharmacologic and Pharmacologic Treatment and BP Goals*

Nonpharmacologic interventions for adults with elevated BP or hypertension

- Weight loss in adults who are overweight or obese (class I recommendation; level of evidence: A)
- A heart-healthy diet (e.g., DASH) to reduce BP (class I recommendation; level of evidence: A)
- Sodium reduction (class I recommendation; level of evidence: A)
- Potassium supplementation, preferably by dietary modification (class I recommendation; level of evidence: A)
- Increased physical activity with a structured exercise program (class I recommendation; level of evidence: A)
- Abstinence from or moderation in alcohol consumption (women, ≤1 standard drink per day; men, ≤2 standard drinks per day) (class I recommendation; level of evidence: A)

Hypertension: 2017 ACC/AHA

Table 1. Classification of BP*

Category	BP
Normal	<120/80 mm Hg
Elevated	120-129/<80 mm Hg
Stage 1 hypertension	130-139/80-89 mm Hg
Stage 2 hypertension	≥140/90 mm Hg

BP = blood pressure.
* Based on accurate measurements and average of ≥2 readings on ≥2 occasions.

TABLE 23 BP Thresholds for and Goals of Pharmacological Therapy in Patients With Hypertension According to Clinical Conditions

Clinical Condition(s)	BP Threshold, mm Hg	BP Goal, mm Hg
General		
Clinical CVD or 10-year ASCVD risk ≥10%	≥130/80	<130/80
No clinical CVD and 10-year ASCVD risk <10%	≥140/90	<130/80
Older persons (≥65 years of age; noninstitutionalized, ambulatory, community-living adults)	≥130 (SBP)	<130 (SBP)
Specific comorbidities		
Diabetes mellitus	≥130/80	<130/80
Chronic kidney disease	≥130/80	<130/80
Chronic kidney disease after renal transplantation	≥130/80	<130/80
Heart failure	≥130/80	<130/80
Stable ischemic heart disease	≥130/80	<130/80
Secondary stroke prevention	≥140/90	<130/80
Peripheral artery disease	≥130/80	<130/80

ASCVD indicates atherosclerotic cardiovascular disease; BP, blood pressure; CVD, cardiovascular disease; and SBP, systolic blood pressure.

Hypertension Guidelines 2017

10.3. Age-Related Issues

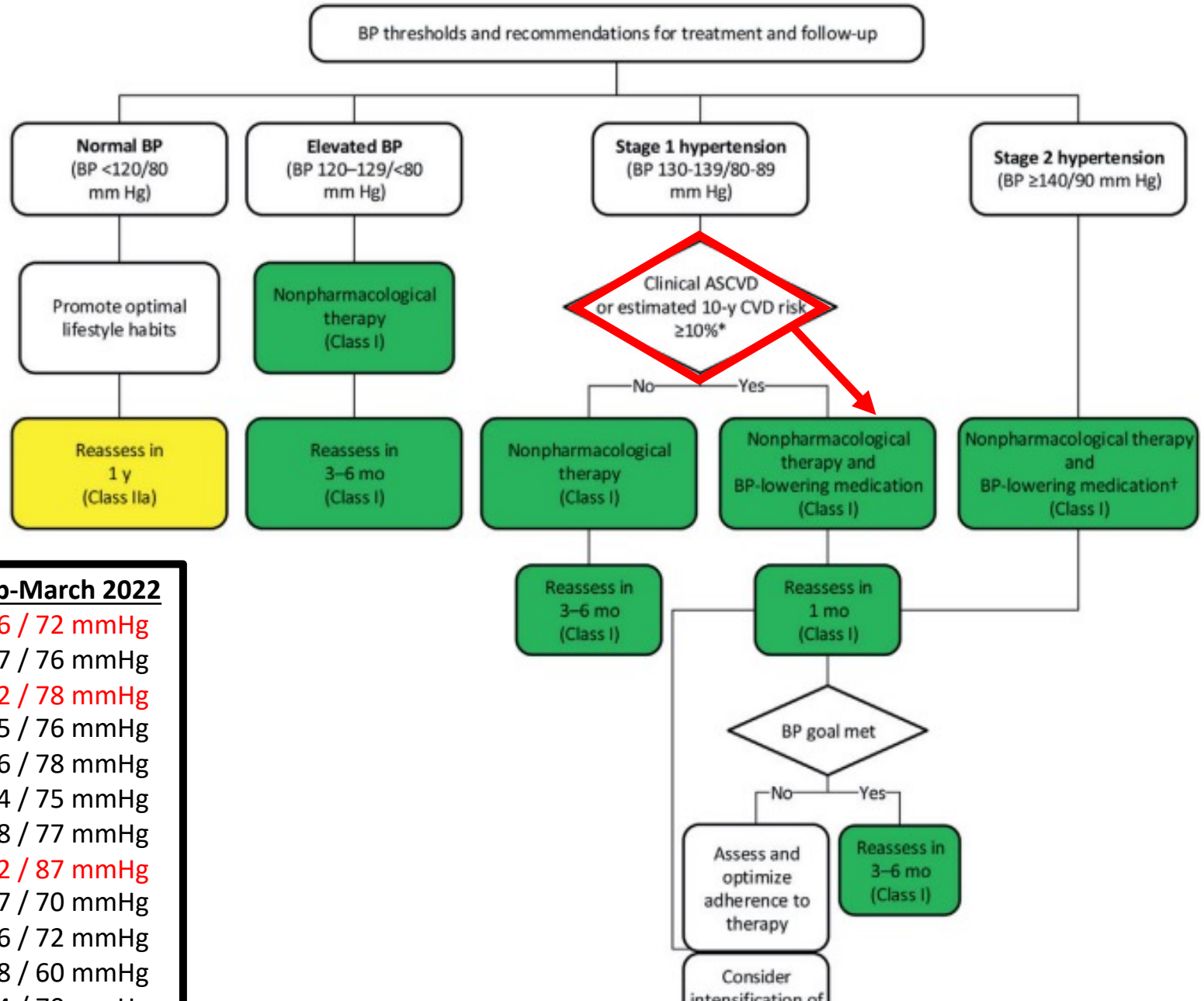
10.3.1. Older Persons

Recommendations for Treatment of Hypertension in Older Persons
References that support recommendations are summarized in Online Data Supplement 54.

COR	LOE	RECOMMENDATIONS
I	A	1. Treatment of hypertension with a SBP treatment goal of less than 130 mm Hg is recommended for noninstitutionalized ambulatory community-dwelling adults (≥65 years of age) with an average SBP of 130 mm Hg or higher (10.3.1.1).
IIa	C-EO	2. For older adults (≥65 years of age) with hypertension and a high burden of comorbidity and limited life expectancy, clinical judgment, patient preference, and a team-based approach to assess risk/benefit is reasonable for decisions regarding intensity of BP lowering and choice of antihypertensive drugs.

2. Patients with prevalent and frequent falls, advanced cognitive impairment, and multiple comorbidities may be at risk of adverse outcomes with intensive BP lowering, especially when they require multiple BP-lowering medications. Older persons in this category typically reside in nursing homes and assisting living facilities, are unable to live independently in the community, and have not been represented in RCTs.

FIGURE 4 Blood Pressure (BP) Thresholds and Recommendations for Treatment and Follow-Up



Feb-March 2022

136 / 72 mmHg
127 / 76 mmHg
132 / 78 mmHg
125 / 76 mmHg
126 / 78 mmHg
124 / 75 mmHg
128 / 77 mmHg
132 / 87 mmHg
127 / 70 mmHg
126 / 72 mmHg
118 / 60 mmHg

BP Treatment

Initiating antihypertensive drug therapy

First-line antihypertensive drugs include thiazide diuretics, CCBs, and ACEIs or ARBs (class I recommendation; level of evidence: A)

Initiate antihypertensive drug therapy in stage 2 hypertension with 2 first-line agents with different mechanisms of action (class I recommendation; level of evidence: C-EO)

Initiate antihypertensive drug therapy in stage 1 hypertension and BP goal <130/80 mm Hg with monotherapy (class IIa recommendation; level of evidence: C-EO)

Statin and Lipid Management

CHOLESTEROL CLINICAL PRACTICE GUIDELINES

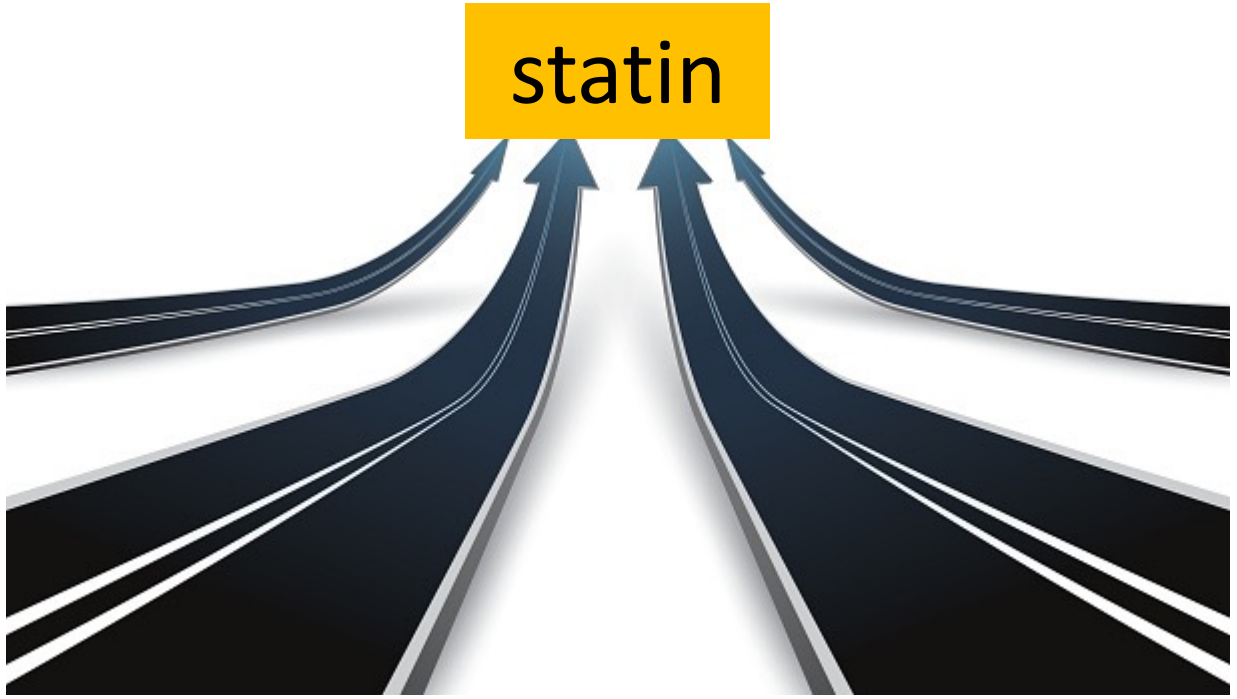
2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Circulation. 2019;139:e1082–e1143. DOI: 10.1161/CIR.0000000000000625

Hyperlipidemia

Recommendations for Adults With High Blood Cholesterol Referenced studies that support recommendations are summarized in Online Data Supplements 11 and 12.		
COR	**LOE**	**Recommendations**
I	A	1. In adults at intermediate risk (≥7.5% to <20% 10-year ASCVD risk), statin therapy reduces risk of ASCVD, and in the context of a risk discussion, if a decision is made for statin therapy, a moderate-intensity statin should be recommended.[S4.3-2–S4.3-9] Adapted from recommendations in the 2018 Cholesterol Clinical Practice Guidelines.[S4.3-1]
I	A	2. In intermediate risk (≥7.5% to <20% 10-year ASCVD risk) patients, LDL-C levels should be reduced by 30% or more, and for optimal ASCVD risk reduction, especially in patients at high risk (≥20% 10-year ASCVD risk), levels should be reduced by 50% or more.[S4.3-2,S4.3-5–S4.3-10] Adapted from recommendations in the 2018 Cholesterol Clinical Practice Guidelines.[S4.3-1]



Statins

*Limited life span may prevent the minimum time for likely statin benefits: 4 to 5 years associated with statins' stroke-reducing benefits

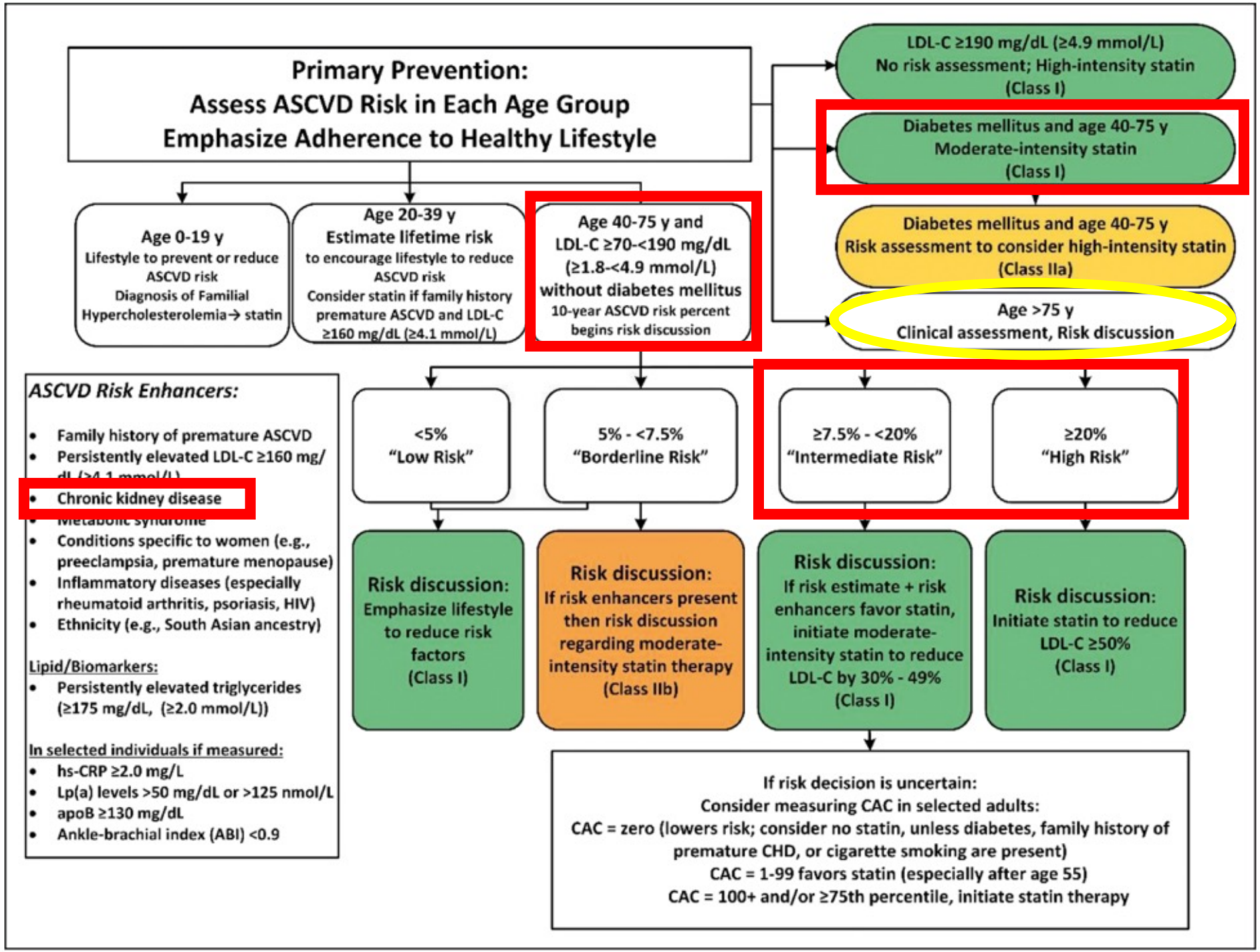
Table. Classification of Statin Therapies

Statin	High-Intensity	Moderate-Intensity	Low-Intensity
	Lowers LDL >50%	Lowers LDL 30% to 49%	Lowers LDL <30%
Atorvastatin	40 mg – 80 mg	10 mg – 20 mg	
Rosuvastatin	20 mg – 40 mg	5 mg – 10 mg	
Lovastatin		40 mg	20 mg
Simvastatin		20 mg – 40 mg	10 mg
Pravastatin		40 mg – 80 mg	10 mg – 20 mg
Fluvastatin (XL)		80 mg	
Fluvastatin		40 mg (twice daily)	20 mg – 40 mg
Pitavastatin		2 mg – 4 mg	1 mg

LDL=low-density lipoprotein.
Source: *Circulation*. 2013;129(25 suppl 2):S1-S45.

Table S5. Common Medications That May Potentially Interact With Statins

Can Be Used With a Statin Using a Risk-Mitigation Strategy*		Do Not Use With Any Statin
• Amiodarone • Amlodipine • Atazanavir plus ritonavir • Boceprevir • Clarithromycin • Cobicistat-containing products • Colchicine • Cyclosporine • Danazol • Darunavir plus ritonavir • Diltiazem • Dronedarone • Erythromycin • Fenofibrate • Fenofibric acid • Fluconazole • Fosamprenavir (with or without ritonavir)	• Itraconazole • Ketoconazole • Lomitapide • Lopinavir plus ritonavir • Nefazodone • Nelfinavir • Niacin (≥1 g/d) • Posaconazole • Ranolazine • Rifampin • Saquinavir plus ritonavir • Telaprevir • Telithromycin • Tipranavir plus ritonavir • Verapamil • Voriconazole • Warfarin	Gemfibrozil


Primary Prevention:
Assess ASCVD Risk in Each Age Group
Emphasize Adherence to Healthy Lifestyle
Age 0-19 y
Lifestyle to prevent or reduce ASCVD risk
Diagnosis of Familial Hypercholesterolemia→ statin
Age 20-39 y
Estimate lifetime risk
to encourage lifestyle to reduce ASCVD risk
Consider statin if family history premature ASCVD and LDL-C ≥160 mg/dL (≥4.1 mmol/L)
Age 40-75 y and LDL-C ≥70-<190 mg/dL (≥1.8-<4.9 mmol/L) without diabetes mellitus
10-year ASCVD risk percent begins risk discussion
LDL-C ≥190 mg/dL (≥4.9 mmol/L)
No risk assessment; High-intensity statin
(Class I)
Diabetes mellitus and age 40-75 y
Moderate-intensity statin
(Class I)
Diabetes mellitus and age 40-75 y
Risk assessment to consider high-intensity statin
(Class IIa)
Age >75 y
Clinical assessment, Risk discussion
ASCVD Risk Enhancers:
Family history of premature ASCVD
Persistently elevated LDL-C ≥160 mg/
Chronic kidney disease
Conditions specific to women (e.g., preeclampsia, premature menopause)
Inflammatory diseases (especially rheumatoid arthritis, psoriasis, HIV)
Ethnicity (e.g., South Asian ancestry)
Lipid/Biomarkers:
Persistently elevated triglycerides (≥175 mg/dL, (≥2.0 mmol/L))
In selected individuals if measured:
hs-CRP ≥2.0 mg/L
Lp(a) levels >50 mg/dL or >125 nmol/L
apoB ≥130 mg/dL
Ankle-brachial index (ABI) <0.9
<5%
"Low Risk"
5% - <7.5%
"Borderline Risk"
≥7.5% - <20%
"Intermediate Risk"
≥20%
"High Risk"
Risk discussion:
Emphasize lifestyle to reduce risk factors
(Class I)
Risk discussion:
If risk enhancers present then risk discussion regarding moderate-intensity statin therapy
(Class IIb)
Risk discussion:
If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LDL-C by 30% - 49%
(Class I)
Risk discussion:
Initiate statin to reduce LDL-C ≥50%
(Class I)
If risk decision is uncertain:
Consider measuring CAC in selected adults:
CAC = zero (lowers risk; consider no statin, unless diabetes, family history of premature CHD, or cigarette smoking are present)
CAC = 1-99 favors statin (especially after age 55)
CAC = 100+ and/or ≥75th percentile, initiate statin therapy

Primary Prevention: Statin in the Elderly

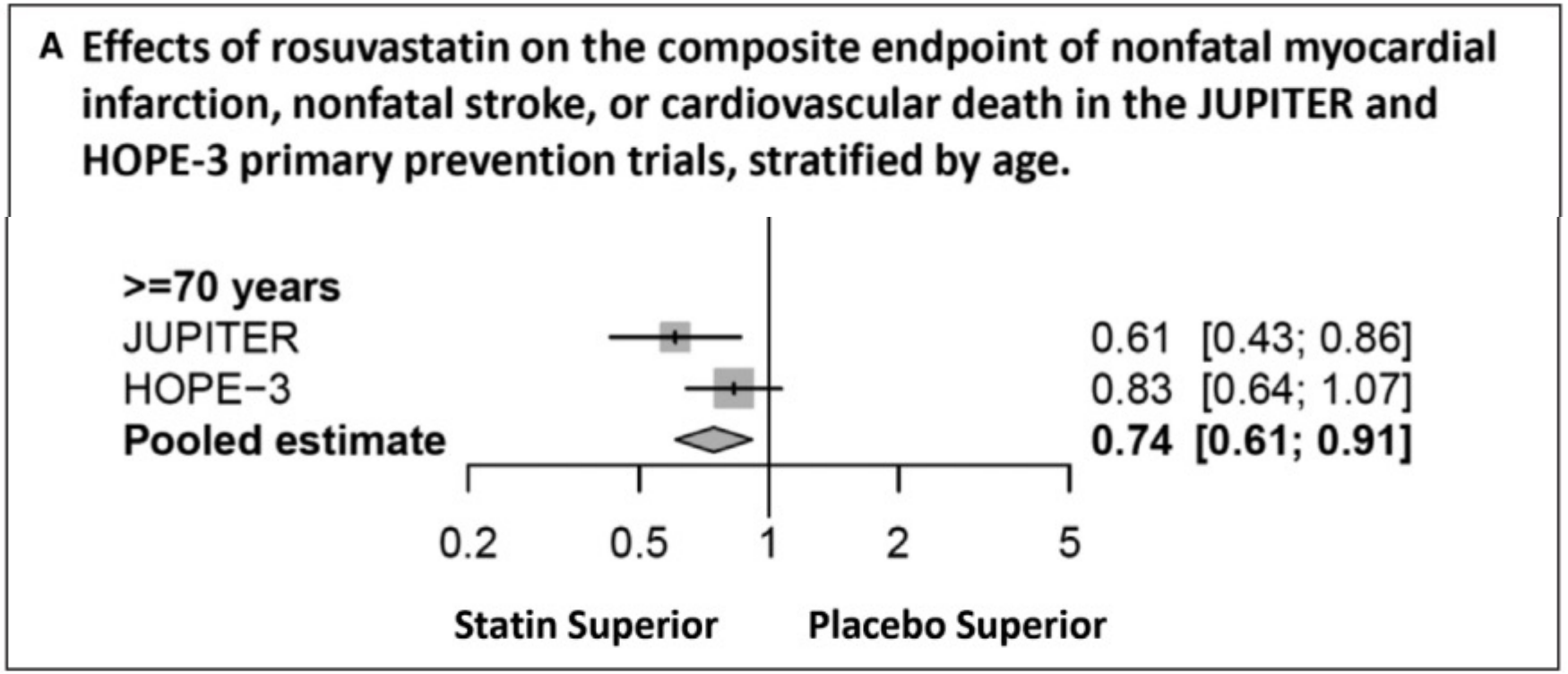


Figure. Rosuvastatin in the JUPITER (Justification for Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin) and HOPE-3 (Heart Outcomes Prevention Evaluation) primary prevention trials.
A, Numbers of individuals at risk, incidence rates, and hazard ratios for nonfatal myocardial infarction, nonfatal stroke, or cardiovascular death in the JUPITER[2] and HOPE-3[3] primary prevention trials, stratified by age. **B**, Meta-analysis within age subgroups of the JUPITER[2] and HOPE-3[3] primary prevention trials evaluating the effects of rosuvastatin on the composite end point of nonfatal myocardial infarction, nonfatal stroke, or cardiovascular death.

Circulation. 2017;135:1979–1981. DOI: 10.1161/CIRCULATIONAHA.117.028271

Primary Prevention

4.3. Diabetes Mellitus in Adults

Recommendations for Patients With Diabetes Mellitus Referenced studies that support recommendations are summarized in Online Data Supplements 11 and 12.		
COR	**LOE**	**Recommendations**
I	A	1. In adults 40 to 75 years of age with diabetes mellitus, regardless of estimated 10-year ASCVD risk, moderate-intensity statin therapy is indicated.[S4.3-1–S4.3-9]

Recommendations for Patients With Diabetes Mellitus (Continued)		
COR	**LOE**	**Recommendations**
IIa	B-NR	2. In adults 40 to 75 years of age with diabetes mellitus and an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), it is reasonable to assess the 10-year risk of a first ASCVD event by using the race and sex-specific PCE to help stratify ASCVD risk.[S4.3-10,S4.3-11]
IIa	B-R	3. In adults with diabetes mellitus who have multiple ASCVD risk factors, it is reasonable to prescribe high-intensity statin therapy with the aim to reduce LDL-C levels by 50% or more
IIa	B-NR	4. In adults older than 75 years of age with diabetes mellitus and who are already on statin therapy, it is reasonable to continue statin therapy.[S4.3-5,S4.3-8,S4.3-13]
IIb	C-LD	5. In adults with diabetes mellitus and 10-year ASCVD risk of 20% or higher, it may be reasonable to add ezetimibe to maximally tolerated statin therapy to reduce LDL-C levels by 50% or more.[S4.3-14,S4.3-15]
IIb	C-LD	6. In adults older than 75 years with diabetes mellitus, it may be reasonable to initiate statin therapy after a clinician–patient discussion of potential benefits and risks.[S4.3-5,S4.3-8,S4.3-13]
IIb	C-LD	7. In adults 20 to 39 years of age with diabetes mellitus that is either of long duration (≥10 years of type 2 diabetes mellitus, ≥20 years of type 1 diabetes mellitus), albuminuria (≥30 mcg of albumin/mg creatinine), estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m², retinopathy, neuropathy, or ankle-brachial index (ABI; <0.9), it may be reasonable to initiate statin therapy.[S4.3-5,S4.3-6,S4.3-8,S4.3-16–S4.3-25]

Table 5. Diabetes-Specific Risk Enhancers That Are Independent of Other Risk Factors in Diabetes Mellitus

Risk Enhancers
Long duration (≥10 years for type 2 diabetes mellitus[S4.3-20] or ≥20 years for type 1 diabetes mellitus[S4.3-6]
Albuminuria ≥30 mcg of albumin/mg creatinine[S4.3-25]
eGFR <60 mL/min/1.73 m²[S4.3-25]
Retinopathy[S4.3-19]
Neuropathy[S4.3-16]
ABI <0.9[S4.3-22,S4.3-24]

Primary Prevention
Age > 75

4.4.4. Primary Prevention in Other Age Groups

4.4.4.1. Older Adults

Additional recommendations for adults >75 years of age are included in Section 4.1. (Secondary ASCVD Prevention) and Section 4.3. (Diabetes Mellitus in Adults).

Recommendations for Older Adults

Referenced studies that support recommendations are summarized in Online Data Supplements 18 and 19.

COR	LOE	Recommendations
IIb	B-R	1. In adults 75 years of age or older with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), initiating a moderate-intensity statin may be reasonable[S4.4.4.1-1–S4.4.4.1-8]
IIb	B-R	2. In adults 75 years of age or older, it may be reasonable to stop statin therapy when functional decline (physical or cognitive), multimorbidity, frailty, or reduced life-expectancy limits the potential benefits of statin therapy.[S4.4.4.1-9]
IIb	B-R	3. In adults 76 to 80 years of age with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), it may be reasonable to measure CAC to reclassify those with a CAC score of zero to avoid statin therapy.[S4.4.4.1-10,S4.4.4.1-11]

4.5.4. Adults With CKD

Recommendations for Adults With CKD

Referenced studies that support recommendations are summarized in Online Data Supplements 36 to 38.

COR	LOE	Recommendations
IIa	B-R	1. In adults 40 to 75 years of age with LDL-C 70 to 189 mg/dL (1.7 to 4.8 mmol/L) who are at 10-year ASCVD risk of 7.5% or higher, CKD not treated with dialysis or kidney transplantation is a risk-enhancing factor and initiation of a moderate-intensity statin or moderate-intensity statins combined with ezetimibe can be useful.[S4.5.4-1,S4.5.4-2]
IIb	C-LD	2. In adults with advanced kidney disease that requires dialysis treatment who are currently on LDL-lowering therapy with a statin, it may be reasonable to continue the statin.[S4.5.4-2]
III: No Benefit	B-R	3. In adults with advanced kidney disease who require dialysis treatment, initiation of a statin is not recommended.[S4.5.4-3,S4.5.4-4]

Aspirin

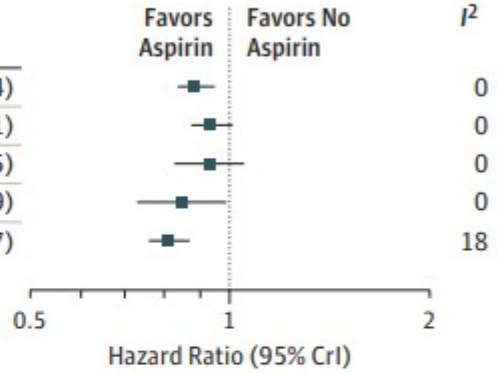
Association of Aspirin Use for Primary Prevention With Cardiovascular Events and Bleeding Events

A Systematic Review and Meta-analysis

ASCEND Trial

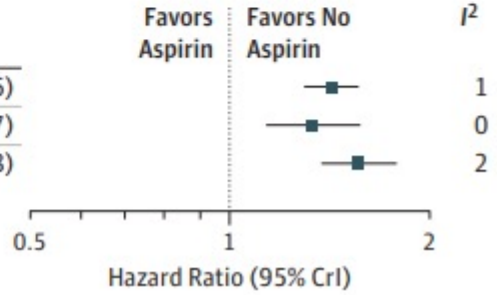
Figure 1. Cardiovascular and Bleeding Outcomes in All Participants

Cardiovascular Outcomes	No. of Studies	Aspirin		No Aspirin		Absolute Risk Reduction, % (95% CI)	HR (95% CrI)
		No. of Events	No. of Participants	No. of Events	No. of Participants		
Composite CV outcome	13	2911	79717	3342	80057	0.41 (0.23 to 0.59)	0.89 (0.84-0.94)
All-cause mortality	13	3622	81623	3588	80057	0.13 (-0.07 to 0.32)	0.94 (0.88-1.01)
CV mortality	13	995	81623	997	80057	0.07 (-0.04 to 0.17)	0.94 (0.83-1.05)
Myocardial infarction	13	1469	81623	1599	80057	0.28 (0.05 to 0.47)	0.85 (0.73-0.99)
Ischemic stroke	10	831	65316	942	63752	0.19 (0.06 to 0.30)	0.81 (0.76-0.87)



NNT: 240

Bleeding Outcomes	No. of Studies	Aspirin		No Aspirin		Absolute Risk Increase, % (95% CI)	HR (95% CrI)
		No. of Events	No. of Participants	No. of Events	No. of Participants		
Major bleeding	11	1195	74715	834	73143	0.47 (0.34 to 0.62)	1.43 (1.30-1.56)
Intracranial bleeding	12	349	80985	257	79419	0.11 (0.04 to 0.18)	1.34 (1.14-1.57)
Major GI bleeding	10	593	70336	380	70465	0.30 (0.20 to 0.41)	1.56 (1.38-1.78)



NNH: 210

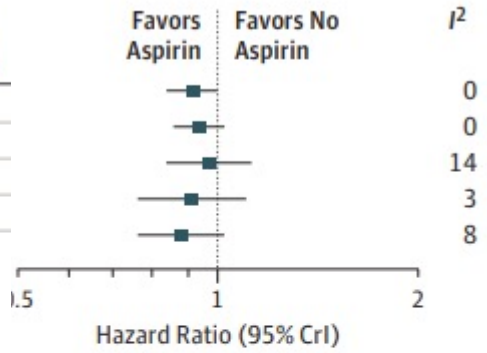
JAMA. 2019;321(3):277-287. doi:10.1001/jama.2018.20578

ASA Primary Prevention Subgroups

B Participants with high CV risk

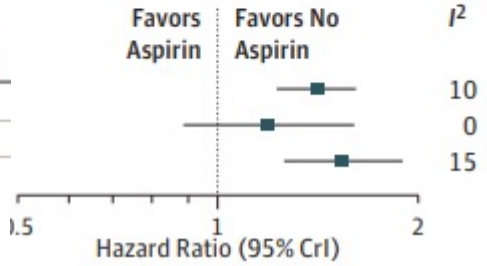
ASCVD risk >10%

Cardiovascular Outcomes	No. of Studies
Composite CV outcome[a]	8
All-cause mortality	7
CV mortality	7
Myocardial infarction[a]	8
Ischemic stroke[a]	6



NNT=159

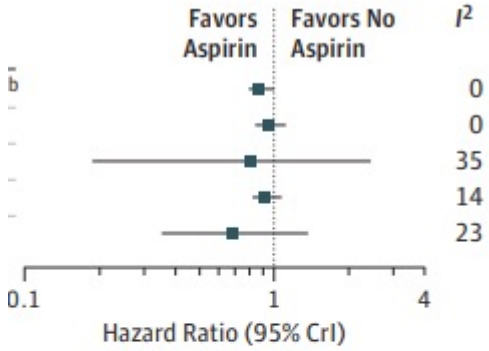
Bleeding Outcomes	No. of Studies
Major bleeding	6
Intracranial bleeding	6
Major GI bleeding	5



NNH=156

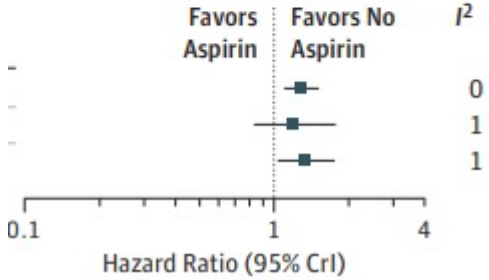
C Participants with diabetes

Cardiovascular Outcomes	No. of Studies
Composite CV outcome	8
All-cause mortality	5
CV mortality	4
Myocardial infarction	8
Ischemic stroke	3



NNT=154

Bleeding Outcomes	No. of Studies
Major bleeding	3
Intracranial bleeding	2
Major GI bleeding	2

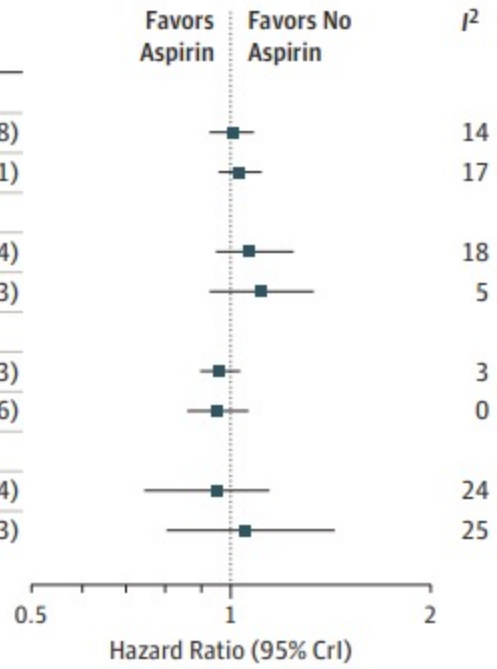


NNH=125

ASA Primary Prevention Cancer Outcomes

Figure 3. Exploratory Cancer Outcomes

Efficacy	No. of Studies	Aspirin		No Aspirin		Absolute Risk Difference, % (95% CI)	HR (95% CrI)	I^2
		No. of Events	No. of Participants	No. of Events	No. of Participants			
All participants								
Incident cancer	10	4507	63048	4409	61475	0.03 (-0.37 to 0.46)	1.01 (0.93-1.08)	14
Cancer mortality	12	1530	75353	1447	73781	0.05 (-0.11 to 0.23)	1.03 (0.96-1.11)	17
Low CV risk participants								
Incident cancer	4	2837	38905	2730	39044	0.41 (-0.13 to 1.01)	1.06 (0.95-1.24)	18
Cancer mortality	5	823	49942	748	50078	0.16 (-0.06 to 0.42)	1.11 (0.93-1.33)	5
High CV risk participants								
Incident cancer	6	1670	24143	1679	22431	-0.30 (-0.76 to 0.19)	0.96 (0.90-1.03)	3
Cancer mortality	7	707	25411	699	23703	-0.13 (-0.41 to 0.17)	0.96 (0.86-1.06)	0
Participants with diabetes								
Incident cancer	3	1091	9640	1116	9655	-0.68 (-2.09 to 0.95)	0.95 (0.74-1.14)	24
Cancer mortality	4	445	10667	438	10685	0.16 (-0.56 to 1.02)	1.05 (0.80-1.43)	25

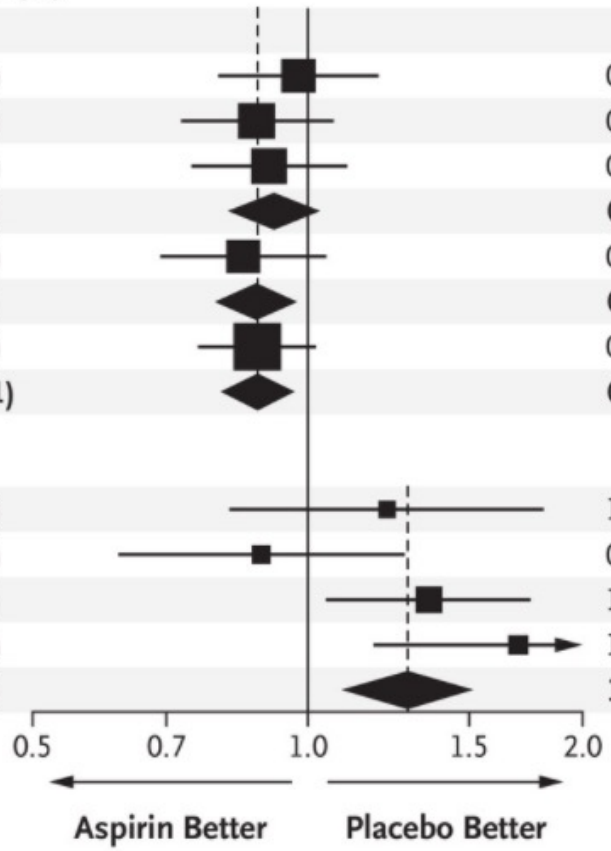


Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus

N Engl J Med 2018;379:1529-39.
DOI: 10.1056/NEJMoa1804988

The ASCEND Study Collaborative Group*

Type of Event	Aspirin (N=7740)	Placebo (N=7740)	Rate Ratio (95% CI)	P Value
	no. of participants with event (%)			
Vascular Outcomes				
Nonfatal myocardial infarction	191 (2.5)	195 (2.5)	0.98 (0.80–1.19)	
Nonfatal presumed ischemic stroke	202 (2.6)	229 (3.0)	0.88 (0.73–1.06)	
Vascular death excluding intracranial hemorrhage	197 (2.5)	217 (2.8)	0.91 (0.75–1.10)	
Any serious vascular event excluding TIA	**542 (7.0)**	**587 (7.6)**	**0.92 (0.82–1.03)**	
TIA	168 (2.2)	197 (2.5)	0.85 (0.69–1.04)	
Any serious vascular event including TIA	**658 (8.5)**	**743 (9.6)**	**0.88 (0.79–0.97)**	**0.01**
Any arterial revascularization	340 (4.4)	384 (5.0)	0.88 (0.76–1.02)	
Any serious vascular event or revascularization	**833 (10.8)**	**936 (12.1)**	**0.88 (0.80–0.97)**	
Major Bleeding				
Intracranial hemorrhage	55 (0.7)	45 (0.6)	1.22 (0.82–1.81)	
Sight-threatening bleeding in eye	57 (0.7)	64 (0.8)	0.89 (0.62–1.27)	
Serious gastrointestinal bleeding	137 (1.8)	101 (1.3)	1.36 (1.05–1.75)	
Other major bleeding	74 (1.0)	43 (0.6)	1.70 (1.18–2.44)	
Any major bleeding	**314 (4.1)**	**245 (3.2)**	**1.29 (1.09–1.52)**	**0.003**



NNT=114

NNH=78

ASPREE: Aspirin in Reducing Events in the Elderly

- Age 70+
- No ASCVD
- 19,000 X 5 years

Conclusions

- significantly higher risk of major hemorrhage without significantly lower risk of cardiovascular disease
- subgroup analysis of CKD did not improve outcomes in older adults
- higher all-cause mortality among older adults taking aspirin than placebo

N Engl J Med. 2018 Oct 18;379(16):1519-1528.
N Engl J Med.2018 Oct 18;379(16):1509-1518.
Kidney Int. 2021 Feb;99(2):466-474.

Aspirin Use

Recommendations for Aspirin Use		
COR	**LOE**	**Recommendations**
IIb	A	1. Low-dose aspirin (75-100 mg orally daily) might be considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk.
III: Harm	B-R	2. Low-dose aspirin (75-100 mg orally daily) should not be administered on a routine basis for the primary prevention of ASCVD among adults >70 years of age.
III: Harm	C-LD	3. Low-dose aspirin (75-100 mg orally daily) should not be administered for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding.

Take Home Message: Primary Prevention

- If institutionalized or > 75 yo: risk discussion
- No ASA for primary prevention
- All HTN targets are < 130/80
- ASCVD risk calculation dictates statin use
  - Older age limits use
- Statin
  - Recommended for Age < 75, T2DM
  - Risk discussion frailty, age >75

Case 1

79 yo Caucasian female, moderate dementia, osteoporosis, residing in NH. Never smoker. Ambulates with wheelchair. DMII diet controlled without complications. On donepezil, alendronate, vitamin D. Weight 74 kg; BMI 26; BP 132/84; TC 180; HDL 50; LDL 110; Hgb A1C 7.2

➢ **10 yr ASCVD 43%**

- 1° vs 2° prevention? 1° prevention
- Lifestyle modifications? Increase exercise, weight loss increases mortality
- HTN Rx? ACC/AHA risk discussion; AMDA not recommended
- T2DM Rx? ACC/AHA risk discussion; If asymptomatic, treatment unlikely to benefit given life expectancy
- ASA? No. Increased bleeding, not for 1° prevention
- Statin? ACC/AHA risk discussion. Treatment unlikely to benefit given life expectancy

Case 2

72 yo Caucasian female, residing in NH. Never smoker. Bipolar, seizure disorder, ambulatory with recurrent falls. On antipsychotic, sertraline, levetiracetam. Weight 65 kg; BMI 22; BP 130/74; TC 210; HDL 60; LDL 126

- **10 yr ASCVD 12%**

- Lifestyle modifications? Increase exercise, weight loss increases mortality
- HTN Rx? ACC/AHA risk discussion: orthostatics/falls
- ASA? No. Increased bleeding, not for 1° prevention
- Statin? ACC/AHA yes moderate intensity. Antipsychotic increased risk of HLD

Questions?